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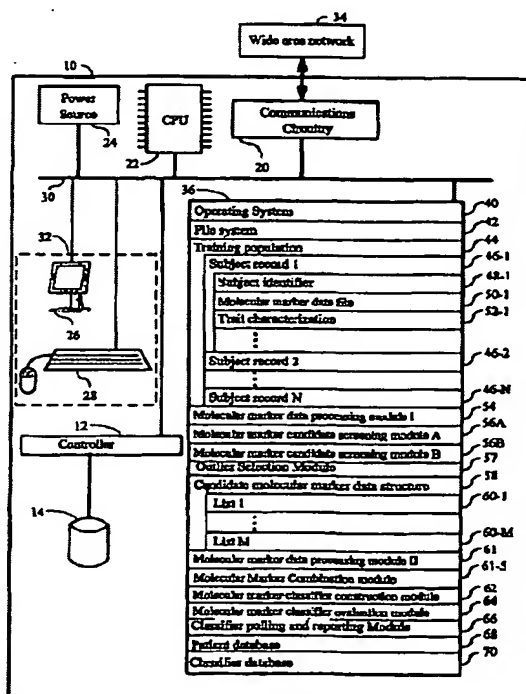
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(54) Title: COMPUTER SYSTEMS AND METHODS FOR CONSTRUCTING BIOLOGICAL CLASSIFIERS AND USES THEREOF



(57) Abstract: The present invention provides systems and method for constructing classifiers that distinguish between trait subgroups using molecular marker data from blood samples. The invention further encompasses the use of the classifiers and combinations of molecular markers identified by the classifiers in a wide variety of applications including: diagnosis; prognosis; prediction of disease, stage of disease or disease risk; monitoring disease progression and/or regression; monitoring disease reoccurrence and identifying risk of disease reoccurrence; determining and/or predicting response to treatment and/or treatment outcomes; monitoring and/or predicting treatment compliance or non compliance and the like. The invention further provides a variety of selected molecular markers and a means to identify combinations of the selected molecular markers useful for diagnosing particular traits of interest.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/22071

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C12Q 1/00(2006.01);G01N 33/48(2006.01)
C12Q 1/00(2006.01);G01N 33/48(2006.01)

USPC: 435/4;702/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/4, 702/19

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/0104499 A1 (PRESSMAN et al.) 05 June 2003 (05.06.2003), page 9, paragraph 0083-0085, page 35, paragraph 0366; page 10 paragraph 0092; page 28, paragraph 0265-0266; pages 35-36, paragraph 0376; page 14, paragraph 0127; page 30, paragraph 0313-0315, 0304, 0307; page 11, paragraph 0098; page 36, paragraph 0397; page 32, paragraph 0329; page 28; paragraph 0262; page 10, paragraph 0094.	1-5, 8-11, 13-20, 22-28, 31, 33-36, 79, 80
Y		6, 7, 12, 21, 29, 30, 32
Y	US 2004/0110221 A1 (TWINE et al.) 10 June 2004 (10.06.2004), page 72, paragraph 0599; page 64; paragraph 0513-0514.	6, 7, 21, 29, 30
Y	US 2003/0073083 A1 (TAMAYO et al.) 17 April 2003 (17.04.2003), page 23, paragraph 0186.	12

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search
16 March 2006 (16.03.2006)

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INTERNATIONAL SEARCH REPORT

International application No.

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-36, 79 and 80

- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-36, 79 and 80, drawn to a method of screening molecular markers by selecting a plurality of markers based on the molecular marker's ability to discriminate.

Group 2, claim(s) 37-77 and 81, drawn to a method of identifying classifiers for a trait by selecting for molecular markers in Tables 1-A-7I.

The inventions listed as Groups 1 and 2 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:
Group 1 has the special technical feature of selecting a plurality of candidate molecular markers based on the molecular marker's ability to discriminate between members of different traits. In contrast, Group 2, has the special technical feature of selecting molecular markers from Tables 1A-7I. Thus the Groups do not share a special technical feature and do not relate to a single general inventive concept under PCT Rule 13.1.

Continuation of B. FIELDS SEARCHED Item 3:

WEST, Medline, Embase, Prosis

Terms: classifier, molecular, marker, population, differential, wald, wolfowitz, mann, whitney, kolmogorov, smirnov, manduchis, database, combination, array, microarray, PCR, differential, rank, subspace, bagging, boosting